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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,018	ROBL ET AL.	
	Examiner	Art Unit	
	Thai-An N Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment, filed 2/9/04, has been entered. Claims 36-52 are pending and under current examination.

Any rejection made of record in the prior Office action, mailed 7/1/03, and not made of record in the instant Office action, has been withdrawn in view of Applicants' arguments and/or amendments to the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 36-52 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-19, 21-25, 32-57, 60 and 61 of copending Application No. 09/260,468.

Applicants argue that the instant claims are directed to a patentably distinct species claimed in the '468 Application because the instant claims are directed to

chimeric proliferating cells containing human DNA and bovine mitochondrial DNA, whereas the '468 application is directed to cross-species NT of a human cell or DNA into any enucleated animal oocytes.

This rejection is maintained for reasons of record. The claims in the '468 application specifically recite the insertion of a human or mammalian cell into an enucleated oocytes, and in further embodiments, a bovine oocytes. See, for example, claims 53-56. Thus, although the conflicting claims are not identical, they are not patentably distinct from each other, because the instant application is directed to a method of cross-species nuclear transfer using differentiated human or mammalian cell or cell nucleus and an enucleated animal oocyte, and the '468 Application is directed to using an adult differentiated human cell or cell nucleus in an enucleated bovine oocyte. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 36-52 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most

nearly connected, to make and/or use the invention is *maintained* for reasons of record.

Applicants argue that the present claims, which are limited to chimeric proliferating cells containing human DNA and bovine mitochondrial DNA provide irrefutable evidence that cross-species NT of a human cell with an enucleated bovine oocytes yielded a NT unit, which in turn proliferated to yield multiple proliferating cells, and this is evidenced by the fact that the disclosed NT unit yielded an embryonic unit with multiple cells. Applicants argue that the Examiner's position that NT embryos may contain both paternal and maternal mtDNA is not disputed, but that the claims merely require that the resulting cells contain human nuclear DNA and maternal (bovine) mtDNA, and that there is no requirement that human mtDNA be absent from the resultant chimeric human/bovine cells. See p. 5-6 of the Response.

This is not found to be persuasive. The prior rejection is based upon the unpredictability of the generation of NT units from cross-species nuclear transfer. Particularly, the specification teaches the production of only one NT unit and fails to show that the method to produce a human/bovine NT unit would be reproducible. Applicants' arguments with regard to the NT unit producing an embryonic unit with multiple cells is not found to be persuasive. The fact that a single NT unit was able to produce multiple cells does not provide evidence that production of the initial NT is reproducible or predictable. The Examiner provides art to support the

unpredictability of the generation of cross-species NT, particularly that even if the claimed invention resulted in a multicellular structure from which an embryo-derived proliferating cell could be isolated and cultured, the mitochondria present in the viable cells would be form the same species as the donor. Applicants have failed to provide teachings or evidence of record to show that the claimed cells have both human nuclear DNA and bovine-derived mtDNA.

Applicants argue that the cells disclosed have numerous disclosed substantial utilities and can be used as donor cells in NT, for transplantation studies, to assay particular cell surface antigens that are expressed at the blastocyst stage, etc. See p. 6, 2nd ¶ of the Response. Applicants further argue that the specification teaches that the disclosed NT process yields NT embryos which divide and proliferate to produce a plurality of proliferating (dividing) cells, and Applicants provide a definition of "proliferate" as evidence. Applicants argue that in contrast to the rejection, it is predictable that cross-species NT can be used to generate chimeric proliferating cells, and that cross-species NT has been used successfully to clone two animals the Gwar and Mouflon. See p. 6, 3rd ¶ of the Response.

Applicants' arguments are not persuasive. Firstly, the references that Applicants allude to have not been provided with the Response, and thus, cannot be considered. Further, the claims require, "embryo-derived proliferating cells", but the specification fails to provide support for what these cells and what their phenotype is. If these cells are not defined by a phenotype, or even what type(s) of

cells they are, one would not know how to use them in the utilities contemplated by Applicants. Applicants argue that the phenotype of the cells is disclosed, and that the phenotype is clear, "an embryonic cell". See p. 7, 1st sentence of the Response. This is not persuasive because the specification fails to teach what "an embryonic cell" is, because there is no teaching or evidence of record as to what "embryo-derived proliferating cells" or "embryonic cells" would be, as the cells are not characterized. The specification teaches that the one NT unit that developed a structure having more than 16 cells was plated down on a fibroblast feeder layer and, "started to propagate forming a colony with ES cell-like morphology", and that the specification concludes that, "Therefore, it is expected that 4-16 cell stage NT units should also give rise to embryonic or stem-like cells and cell colonies." See p. 28, lines 6-14. Thus, the specification fails to provide any evidence or teachings of the type of cell produced from the one NT unit, other than a morphology that resembled ES-like cells. Thus, the specification fails to provide a phenotype, or what type(s) of cells would be encompassed by "embryo-derived proliferating cells" or "embryonic cells".

Applicants argue that the Examiner's comment that the specification does not define which is the "inner portion" of the NT unit is the "inner portion" is indefensible because blastocyst stage embryos have a characteristic morphology and the inner portion is very discernable. See p. 7, 1st ¶ of the Response. This is not persuasive because the specification fails to provide support for what comprises the

inner portion versus portions of the blastocyst which would not be considered the inner portion. Further, there is no teaching or guidance provided by the specification as to which cells would comprise the inner portion.

It is reiterated that, in view of the supported undeveloped and unpredictable state of the art with respect to the characterization of cells produced by cross-species NT, Applicants' demonstration of the production of only one NT unit (Table 1) cannot be extrapolated to the production of embryo-derived cells as known in the art. In the instant case, Applicants fail to provide guidance to the skilled artisan on any parameters which would be necessary and critical for the production of embryo-derived cells having human DNA and bovine-derived mitochondria stem-like cells by the cross-species NT process.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction and/or guidance provided by the specification, the absence of working examples for the demonstration of or reasonable correlation to producing embryo-derived proliferating cells having human DNA and bovine-derived mitochondria, the unpredictable and undeveloped state of the art with respect to cross-species nuclear transfer, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The prior rejection of claims 36-52 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Applicants argue that the inner portion (as noted above) is substantiated by the figures, and that one of skill in the art could readily and easily discern the "inner portion" of an NT unit, and that would be routine to those skilled in the art. See p. 7, 3rd ¶ of the Response. This is not found to be persuasive. This term is vague because neither the claim nor the specification provide a definition for the term "inner portion". For example, which cells make up the inner portion of the NT unit? How many cells are in the inner portion? How much of the NT unit contains the inner portion? Claims 37-50 depend from claim 36. Claim 52 depends from claim 51.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The prior rejection of claims 48, 49, 50 and 52 under 35 U.S.C. 102(b) as being anticipated by Heyneker *et al.* [WO 91/08216, published 13 June 1991] is maintained for reasons of record.

Applicants vigorously traverse this rejection and argue that Heynecker does not teach or suggest the claimed chimeric cells containing the nuclear DNA of a human cell and bovine mitochondrial DNA and that it is an unreasonable interpretation of the claim to suggest that transgenic bovine cells would read on the claims if they are properly construed based upon the teaching of the application. Applicants argue that the claims provide that the cells result from transplantation of a human cell or human cell nucleus into an oocytes. Accordingly, Applicants argue that based upon the means by which the cells are produced, the claims are not anticipated by a transgenic bovine cells containing a human gene. See pp. 7-8 of the Response.

This is not found to be persuasive. The claims are directed to isolated proliferating cells having human nuclear DNA and bovine-derived mitochondria. As stated in the prior Office action, the claims are product-by-process claims and when the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie

obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Applicants have failed to show how the claimed isolated proliferating cells would be different from the cells taught by Heyneker, because the cells taught by Heyneker fulfill the limitations of the claims. Particularly, that the isolated cells have human nuclear DNA and bovine-derived mtDNA. Thus, the bovine cells that contain a human transgene, as taught by Heyneker, anticipate the claimed invention.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

TNT

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